II. REMARKS

Preliminary Remarks:

Claims 1, 3-6, 8 and 9 are amended, claims 11 and 12 are canceled, and new claims 13-15 are added.

Claim 1 is amended to be directed to a method for inducing T-cell tolerance or non-responsiveness of donor T-cells to desired alloantigen-bearing cells wherein the cells are cultured in a mixed lymphocyte reaction culture in the presence of a gp39 antagonist that is an anti-gp39 antibody or a gp39-binding fragment thereof, which method comprises a step of assaying *ex vivo* for induction of donor T-cell tolerance or non-responsiveness. Claims 3-5 and 8 are amended so that they are directed more specifically to the elected invention. New claims 13-15 specify *ex vivo* assay methods disclosed in the specification (see Examples 1-9 on pages 10-14).

Patentability Remarks:

35 U.S.C. §112, first paragraph

The specification was objected to under 35 U.S.C. §112, first paragraph, as failing to provide sufficient written description for culturing for "one to thirty days," and "from 5-15 days" as recited in claims 6 and 7. The specification describes *ex vivo* culture for the time periods in question on page 8, lines 22-29, in the context of describing an embodiment in which the gp39 antagonist is an antibody. The specification further discloses the same time periods in original claims 6 and 7, which are directed to a method in which the gp39 antagonist is referred to in broad terms that include soluble CD40, a soluble CD40 fusion protein, unspecified anti-gp39-antibodies, and gp39-binding antibody fragments, as well as the antibody disclosed on page 8 of the specification. At the time the priority application was filed, a person skilled in the art would reasonably have expected that gp39 antagonists such as soluble CD40, a soluble CD40 fusion protein, and gp39-binding antibody fragments, and anti-gp39-antibodies other than the ones referred to on page 8, would operate in the disclosed

method to induce donor T-cell tolerance or non-responsiveness within approximately the same time periods as those described for the embodiment disclosed on page 8. Furthermore, persons skilled in the art would have regarded the presentation of original claims 6 and 7 in the specification as an affirmative assertion by the applicants that the same time periods disclosed in the discussion of the embodiment on page 8 are also applicable for the broadly claimed invention. Accordingly, a person skilled in the art would reasonably have considered the description of the invention disclosed in the specification to be sufficient to convey that at the time the application was filed, the inventors were in possession of the invention of claims 6 and 7 wherein the recited time periods are applicable for the disclosed method in which the gp39 antagonist includes disclosed gp39 antagonists other than the anti-gp39-antibodies referred to on page 8, such as soluble CD40, a soluble CD40 fusion protein, other anti-gp39-antibodies, and gp39-binding antibody fragments thereof. The applicants therefore respectfully request that the objection for lack of written description be withdrawn.

35 U.S.C. §112, second paragraph

The Applicants respectfully request that the rejection of claim 9 under 35 U.S.C. §112, second paragraph, as being indefinite, be withdrawn in view of the amendment of the claim to specify that recipient T-cell depletion is effected by irradiation. Support for the amendment is found on page 10, lines 12-20.

35 U.S.C. §102(e)

Claims 1-8 and 10-11 were rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 5,876,718 of Noelle et al. Claim 1 is amended to recite a method that includes a step comprising assaying *ex vivo* for induction of donor T-cell tolerance or non-responsiveness. The prior art neither describes nor discloses the claimed invention which comprises such an *ex vivo* assay step. The applicants therefore respectfully request that the rejection of the claims under 35 U.S.C. §102(e) be withdrawn.

35 U.S.C. §103(a)

Claims 1-3 and 6-11 were rejected under 35 U.S.C. §103(a) as being obvious in view of U.S. Patent No. 5,876,718 of Noelle et al., further in view of U.S. Patent No. 5,962,318 of Rooney et al., and Riddel et al. (1990).

Claim 1 is amended to include a step comprising assaying ex vivo for induction of donor T-cell tolerance or non-responsiveness, and claims 13-15 are directed to methods that employ specific, disclosed *ex vivo* assays. Claims 6 and 7 further specify particular time periods during which the T cells become tolerized.

None of the cited prior art references, alone or in combination, describe or suggest the claimed method comprising assaying ex vivo for induction of donor T-cell tolerance or non-responsiveness. Moreover, nothing in the prior art suggests the claimed method that includes assaying ex vivo for induction of donor T-cell tolerance or non-responsiveness by a method comprising measuring and comparing the concentration of IL-2, interferon-gamma, or an antigen selected from the group consisting of L-selectin, ICAM-1, and CD45, in the donor T-cells cultured in step iv and control donor T-cells, as stated in new claims 13-15. Further more, the cited prior art references neither disclose nor suggest the claimed time periods for T cell tolerization in *ex vivo* culture. Accordingly, the applicants request that the rejection of the claims under 35 U.S.C. §103(a) as being obvious in view of the prior art be withdrawn.

Double Patenting

The claims of the present application were rejected under 35 U.S.C. §101 as being directed to the same invention as the claims of co-pending U.S. Application No. 09/835,126, which is the present application. This rejection is treated as being made with regard to the claims of co-pending U.S. Application No. 09/951,537. The applicants respectfully request that the rejection of the claims for double patenting be withdrawn, because the claims of the present application and those of co-pending U.S. Application No. 09/951,537 have been amended to be directed to non-identical inventions.

Conclusion

All rejections having been addressed, it is respectfully submitted that the present application is in condition for allowance and a Notice to that effect is earnestly solicited. If any points remain in issue, which the examiner feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,
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